November 8, 2002

James A. Deyo, D.V.M., Ph.D., D.A.B.T.
Technical Associate
Eastman Chemical Company
P. O. Box 431
Kingsport, Tennessee 37662

Dear Dr. Deyo:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for 1,4-cyclohexanedimethanol, posted on the ChemRTK HPV Challenge Program Web site on July 3, 2002. I commend Eastman Chemical Company for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its HPV Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the attached comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that Eastman Chemical Company advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. Submit questions about the HPV Challenge Program through the "Contact Us" link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

/s/

Oscar Hernandez, Director
Risk Assessment Division

Attachment

cc: C. Auer
A. Abramson
M. E. Weber

EPA Comments on Chemical RTK HPV Challenge Submission:
1,4-Cyclohexanedimethanol

SUMMARY OF EPA COMMENTS

The sponsor, Eastman Chemical Company, submitted a test plan and robust summaries for 1,4-cyclohexanedimethanol (CAS No. 105-08-8) to EPA on June 12, 2002. EPA posted the submission on the Chemical RTK HPV Challenge Web site on July 3, 2002.

EPA has reviewed this submission and has reached the following conclusions:

1. Physicochemical Data. Data are adequate for melting point and boiling point. The submitter needs to provide measured data for vapor pressure and address specific questions on water solubility.

2. Environmental Fate. Data are adequate for photodegradation/atmospheric oxidation, stability in water and transport and distribution. Additional biodegradation testing is needed.

3. Health Effects. Data are acceptable for acute toxicity and adequate for repeated-dose, developmental toxicity and the genetic toxicity endpoint of chromosomal aberrations. A separate robust summary is needed for the reproductive toxicity endpoint. Data may be adequate for the genetic toxicity endpoint of gene mutations, however, enough detail has not been provided.

4. Ecological Effects. The endpoints for fish, aquatic invertebrates, and algae have been addressed for the purposes of the HPV Challenge Program.

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

EPA COMMENTS ON THE 1,4-CYCLOHEXANEDIEMETHANOL CHALLENGE SUBMISSION

Test Plan

Chemistry (melting point, boiling point, vapor pressure, partition coefficient and water solubility).

Vapor pressure. The submitter provided an estimated vapor pressure value of 0.000371 mm Hg (0.049 Pa) using MPBPWIN. Calculated values are acceptable only when the value is less than 10^{-5} Pa at 25 °C (OECD). The submitter needs to provide measured data for this endpoint according to OECD guidelines.

Water solubility. The submitter provided an estimated water solubility value which is much lower than a measured value EPA identified in the literature (Gerhartz,1985). An explanation of this discrepancy is needed.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity).

Biodegradation. The submitter tested the biodegradation of this substance using a Zahn-Wellens/EMPA test for inherent biodegradability that was done in accordance with OECD Guideline 302B. No biodegradation data were found in the literature by the Agency. Inherent biodegradability data can be considered adequate only if a substance does not degrade in such a test. Positive results in inherent tests indicate only that a substance is "not persistent," whereas negative results may be taken to mean that a substance is nonbiodegradable. Positive results are not sufficient to adequately characterize the behavior of the compound in the environment. The submitter needs to provide ready biodegradation data following OECD Guideline 301.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity).

Data are adequate for repeated-dose, developmental toxicity and the genetic toxicity endpoint of chromosomal aberrations. The data for acute toxicity was not adequate but, based on the weight of the evidence, no additional testing is needed for the purposes of the HPV Challenge Program. It appears that

the reproductive endpoint was addressed adequately by the study conducted but an appropriate robust summary was not supplied. Data may be adequate for the genetic endpoint of gene mutations, however, enough detail has not been provided.

Acute toxicity. The study was deficient, as described in the comments on robust summaries section, however, other information available indicates that the substance does not exhibit a high degree of acute toxicity and no further testing is needed.

Reproductive toxicity. A reproductive and developmental toxicity screening test (OECD TG 421) was submitted. Although reproductive effects are mentioned in the robust summary for developmental effects, a separate robust summary is needed for the reproductive toxicity endpoint.

Genotoxicity (gene mutations). The Ames assay was not conducted at a high enough concentration. The maximum concentration used, 500 ug per plate, was one-tenth of the recommended concentration. However, if the substance was tested at this level because of cytotoxicity, then inclusion of information on the levels at which cytotoxicity occurred relevant to the dose selected would be sufficient to satisfy this endpoint. Otherwise, another test is needed.

Ecological Effects (fish, invertebrate and algal toxicity)

Data are adequate for fish and algae. Although the submitter provided a daphnia study of 96-hours rather than a 48-hour study, the study, in this case, is considered adequate to address this endpoint for the purposes of the HPV Challenge Program.

Specific Comments on the Robust Summaries

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity).

Transport and distribution (fugacity). The submitter needs to incorporate the actual input values utilized in its estimation of this endpoint.

Health Effects

Acute toxicity. The purity of the test material was unknown. The age, sex, strain, and body weight of the rats were not given. It is unclear how many animals were tested (10 total or 10 per dose). It was unclear whether the rats were fasted prior to dosing, whether the decedent rat was in the highest dosing group, and if necropsy was performed. In addition, the LD_{50} calculation method was not given.

Reproductive toxicity. A separate robust summary is needed for the reproductive toxicity endpoint. Detailed information is needed for parameters showing effects. Even though effects were reported only at the highest dose level, detailed information concerning these parameters for all dose levels would be useful.

Developmental toxicity. Details are needed for the developmental parameters observed.

Genotoxicity (gene mutations). In addition to the cytotoxicity question identified above, other deficiencies noted were: only one plate was tested per concentration when three are recommended and there was no indication of which positive controls were used with which strains and whether the responses obtained were appropriate.

Followup Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

Reference

Gerhartz,W.(ed.) Ullmann's Encyclopedia of Industrial Chemistry. 5th ed. Volume A1. p. 312. Deerfield Beach, FL:VCH Publishers, 1985.